

Claims

1. Modified fiber of an adenovirus, comprising at least one mutation at one or more residues within the region of said fiber stretching from pleated sheet A to pleated sheet B, and including loop AB.
2. Fiber of an adenovirus according to Claim 1, characterized in that it comprises at least one mutation at one or more residues within loop AB.
3. Fiber of an adenovirus according to Claim 1 or 2, characterized in that it allows, when it is included in a viral particle, the production of a said viral particle having the following properties:
  - (i) said adenoviral particle does not substantially attach to the natural cellular receptors;
  - (ii) when said adenoviral particle also comprises a ligand specific for an antiligand, said modified particle has a novel tropism for one or more specific cell types carrying, at their surface, said antiligand.
4. Fiber of an adenovirus according to one of Claims 1 to 3, characterized in that it derives from a fiber of a type 5 adenovirus (Ad5) comprising all or part of the sequence as shown in sequence identifier No. 1 (SEQ ID NO: 1), and in that it comprises at least one mutation at one or more residues of the region between residues 400 and 428.
5. Fiber of a type 5 adenovirus according to Claim 4, characterized in that it comprises at least one mutation at one or more residues of the region between residues 404 and 418 of SEQ ID NO: 1.
6. Fiber of a type 5 adenovirus according to Claim 5, characterized in that it comprises at least one mutation at one or more residues of the region between residues 404 and 408 of SEQ ID NO: 1.
7. Fiber of a type 5 adenovirus according to Claim 6, characterized in that said residue is selected from the threonine residue at position 404, the alanine

residue at position 406 and the serine residue at position 408.

8. Fiber of a type 5 adenovirus according to Claim 7, characterized in that it comprises substitution of the serine residue at position 408 with an amino acid residue having at least two carboxyl groups.

9. Fiber of a type 5 adenovirus according to Claim 8, characterized in that said residue is selected from the group consisting of aspartic acid and glutamic acid.

10. Fiber of a type 5 adenovirus according to Claim 7, characterized in that it comprises substitution of the threonine residue at position 404 with a glycine residue and/or substitution of the alanine residue at position 406 with a lysine residue.

11. Fiber of an adenovirus according to one of Claims 1 to 10, characterized in that one at least of the mutations is deletion of at least 3 consecutive residues of a loop and/or of a pleated sheet of said region.

12. Fiber of an adenovirus according to Claim 11, characterized in that said deleted residues are replaced with residues of an equivalent loop and/or pleated sheet derived from a fiber of a second adenovirus of heterologous type, capable of interacting with a cellular receptor other than that recognized by said first adenovirus.

13. Fiber of an adenovirus according to one of Claims 1 to 12, characterized in that it also comprises one or more mutations in:

(i) loops CD, DG, GH, HI and/or IJ  
and/or

(ii) pleated sheets C, D, G, H, I and/or J.

14. Fiber of an adenovirus according to one of Claims 1 to 13, characterized in that it also comprises a ligand capable of recognizing a cellular antiligand other than the natural cellular receptor of the nonmutated fiber.

15. Fiber of an adenovirus according to Claim 14, characterized in that the ligand is selected from the group consisting of an antibody or an antibody fragment, a peptide, a lipid, a glycolipid, a hormone, a polymer or a sugar.

16. Fiber of an adenovirus according to Claim 14 or 15, characterized in that the ligand is inserted at the C-terminal end of the fiber.

17. Fiber of an adenovirus according to Claim 14 or 15, characterized in that the ligand is inserted as a replacement for deleted residues.

18. Peptide fragment characterized in that it comprises the region stretching from pleated sheet A to pleated sheet B, and including loop AB, of a fiber according to any one of Claims 1 to 17.

19. Peptide fragment according to Claim 18, characterized in that it is the sequence stretching from residue 388 to residue 592 of a fiber according to any one of Claims 4 to 17.

20. DNA fragment or expression vector encoding a fiber of an adenovirus according to one of Claims 1 to 17, or a peptide fragment according to either of Claims 18 and 19.

21. Cell line characterized in that it comprises, either in a form integrated into the genome or in episome form, a DNA fragment according to Claim 20, placed under the control of the elements allowing its expression in said cell line.

22. Cell line according to Claim 21, characterized in that it is also capable of complementing an adenovirus deficient for one or more functions selected from the functions encoded by the E1, E2, E4 and L1-L5 regions.

23. Cell line according to Claim 21 or 22, characterized in that it is produced using the 293 line.

24. Cell line according to Claim 21 or 22, characterized in that it is produced using the PERC6 line.

25. Adenoviral particle characterized in that it lacks a functional native fiber, and in that it comprises a fiber according to one of Claims 1 to 17.

5 26. Adenoviral particle characterized in that it lacks a functional native fiber, and in that it comprises a fiber according to one of Claims 1 to 17 and a ligand capable of recognizing a cellular antiligand other than the natural cellular receptor for said particle.

10 27. Adenoviral particle according to Claim 26, characterized in that said ligand is inserted into an adenoviral capsid protein other than the fiber, in particular the hexon or the penton.

15 28. Adenoviral particle according to one of Claims 25 to 27, characterized in that it is empty.

29. Adenoviral particle according to one of Claims 25 to 27, characterized in that it contains an adenoviral genome.

20 30. Adenoviral particle according to Claim 29, characterized in that said adenoviral genome is a replication-defective recombinant adenoviral genome.

31. Process for producing an adenoviral particle according to Claim 29, characterized in that:

25 (i) a said replication-defective recombinant adenoviral genome is transfected into a suitable cell line,

30 (ii) said transfected cell line is cultured under suitable conditions so as to allow the production of said adenoviral particle, and

35 (iii) said adenovirus is recovered from the culture of said transfected cell line and, optionally, said adenoviral particle is purified.

32. Process for producing an adenoviral particle containing an adenoviral genome lacking all or part of the sequences encoding a fiber, characterized in that:

- 5       - said genome is transfected into a cell line according to one of Claims 21 to 24,
- said transfected cell line is cultured under suitable conditions so as to allow the
- 10       production of said adenoviral particle, and
- said adenoviral particle is recovered from the culture of said transfected cell line and, optionally, said adenoviral particle is
- 15       purified.

33. Composition which comprises an adenoviral particle according to one of Claims 25 to 30, or which can be obtained using a process according to Claim 31

20 or 32, in combination with a support which is acceptable from a pharmaceutical point of view.

34. Composition according to Claim 33, characterized in that it also comprises at least one compound selected from a naked nucleic acid or a

25 nucleic acid combined with at least one cationic compound.

35. Use of an adenoviral particle according to one of Claims 25 to 30, or which can be obtained using a process according to Claim 31 or 32, for preparing a

30 medicinal product intended for the treatment of the human or animal body.